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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 11/06/2003

Ref

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/306,749

Applicant(s)

MEADE ET AL.

Examiner

Jeffrey Fredman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-22,24 and 25 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 12-22,24 and 25 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Status

1. Claims 12-22, 24 and 25 are pending.

Claims 12-22, 24 and 25 are rejected.

This action is a new, non-final action, on an application which was withdrawn from issue on September 11, 2003.

Claim Interpretation

2. The broadest claim, claim 12, is drawn to "A nucleoside comprising a ribose comprising a covalently attached electron transfer moiety (ETM) at the 2' position wherein said ETM is attached via a linker". This claim is open to several interpretations. First, the term "comprising a ribose" implies that the ribose may have any group attached to it, including an oligonucleotide linked at the 5' position. Therefore, for prior art purposes, this claim will be interpreted to include oligonucleotides which comprise the ribose. Second, even if the claim were closed to "consisting of a ribose", the cited prior art below teaches linking of the substituents to a nucleoside via a linker as discussed in the rejection.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claims 12-16, 22, 24 and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Manoharan et al (U.S. Patent 6,153,737 (102(e) date April 22, 1992)).

Manoharan teaches a nucleoside (as well as nucleotide or oligonucleotide) (see column 7, lines 32-37) comprising a ribose comprising a covalently attached electron transfer moiety (ETM) at the 2' position wherein said ETM is attached via a linker (see column 7, lines 4-16 and 32-37, as well as example 30, column 33, lines 45-67, where a nucleotide is linked at the 2' position to an EDTA FE(II) complex). It is noted that Applicant's specification states "As used herein, the term "nucleoside" includes nucleotides (see page 9, lines 8-9)." Manoharan expressly teaches ETM groups as substituents at column 7, lines 4-16, including phenanthroline/Cu complexes (see line 8) and Ru(bpy) complexes (see line 9). It is noted that the linking groups listed in column 7, lines 32-65 would inherently result in the covalent attachment of the substituents to the nucleotide, nucleoside or nucleic acid as in Example 30 where the EDTA FE(II) complex is covalently attached).

With regard to claim 13, Manoharan teaches organic moieties such as acridine (see column 7, line 22, for example).

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With regard to claim 14, Manoharan teaches transition metal complexes such as EDTA FE(II) and Ru(bpy) and phenanthroline/Cu (see column 7, lines 8-11 and example 30, for example).

With regard to claim 15, Manoharan teaches Ruthenium complexes such as Ru(bpy) (see column 7, line 9, for example).

With regard to claim 16, Manoharan teaches Iron metal complexes (see example 30, for example).

With regard to claim 22, Manoharan teaches the use of amine linkers (see column 7, lines 32-65, for example).

With regard to claim 24, Manoharan teaches nucleotides (see column 7, line 33, for example).

With regard to claim 25, Manoharan teaches nucleic acids (see column 7, line 34 and example 30, for example).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

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under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 12-22, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manoharan et al (U.S. Patent 6,153,737 (102(e) date April 22, 1992)) in view of Burrows et al (U.S. Patent 5,272,056).

Manoharan teaches a nucleoside (see column 7, lines 32-37) comprising a ribose comprising a covalently attached electron transfer moiety (ETM) at the 2' position wherein said ETM is attached via a linker (see column 7, lines 4-16 and 32-37, as well as example 30, column 33, lines 45-67, where a nucleotide is linked at the 2' position to an EDTA FE(II) complex). It is noted that Applicant's specification states "As used herein, the term "nucleoside" includes nucleotides (see page 9, lines 8-9)." Manoharan expressly teaches ETM groups as substituents at column 7, lines 4-16, including phenanthroline/Cu complexes (see line 8) and Ru(bpy) complexes (see line 9). It is noted that the linking groups listed in column 7, lines 32-65 would inherently result in the covalent attachment of the substituents to the nucleotide, nucleoside or nucleic acid as in Example 30 where the EDTA FE(II) complex is covalently attached).

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With regard to claim 22, Manoharan teaches the use of amine linkers (see column 7, lines 32-65, for example).

With regard to claim 24, Manoharan teaches nucleotides (see column 7, line 33, for example).

With regard to claim 25, Manoharan teaches nucleic acids (see column 7, line 34 and example 30, for example).

Manoharan suggests the use of metal complexes (see column 5, line 25, for example) for cleavage of DNA (see column 7, lines 4-16), and Manoharan exemplifies certain metals including Ruthenium, Iron and Copper, but Manoharan does not teach the use of Osmium, Rhenium, Cobalt, Palladium or Platinum.

Burrows teaches the equivalence of a variety of transition metals in cleavage of DNA (see column 3, lines 3-5). Burrows expressly teaches that "The useful transition metals include ions of Ni, Co, Cu, Rh, Pd, Ir, Pt, Cr, Mn, Fe, Ru, and Os (see column 11, lines 36-38)." So Burrows expressly teaches the use of Osmium (Os),

Cobalt (Co), Palladium (Pd), Platinum (Pt) and suggests the equivalence of all transition metals, which would include Rhenium.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the transition metals and cleavage complexes of Burrows in the method of Manoharan since Manoharan states a desire to use groups such as "RNA cleaving complexes, pyrenes, metal chelators (see column 7, line 5)", where "RNA cleavers include o-phenanthroline/Cu complexes and Ru(bipyridine)₃²⁺ complexes. The Ru(bpy)₃²⁺ complexes interact with nucleic acids and cleave nucleic acids photo-chemically (see column 7, lines 7-10)." Thus, Manoharan expressly motivates the use of RNA cleavage groups with transition metals as substituents on the DNA oligonucleotides. Burrows teaches "It is a further object of the invention to provide a method for cleavage of single-strand DNA at guanine sites (see column 3, lines 3-5)." Thus, Burrows motivates the use of the metal complexes for cleavage of nucleic acid and Manoharan expressly desires nucleic acid cleavage compounds linked to DNA for the antisense methods, so an ordinary practitioner would have been motivated to use the additional transition metals of Burrows in the compounds of Manoharan.

Further, Manoharan recognizes the use of transition metals and Burrows teaches the equivalence of these transition metals in nucleic acid cleavage compositions. MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical

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equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)." Consequently, it would have been prima facie obvious to substitute the various equivalent transition metals for each other in the composition of Manoharan since the prior art recognized these metals as equivalents in nucleic acid cleavage as demonstrated by Burrows.

Double Patenting

8. Claims 12-22, 24 and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 5,780,234 in view of Burrows et al (U.S. Patent 5,272,056).

Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 3 of U.S. Patent No. 5,780,234 teaches a composition which comprises a nucleic acid linked at the 2' ribose to an electron transfer moiety. Thus, the composition of claim 3 comprises the compound claimed in claims 12-22, 24 and 25 of the current claim. This compound is therefore an obvious compound to synthesize in order to create the composition of claim 3.

Claim 3 of U.S. Patent No. 5,780,234 does not teach the particular transition metals used in the electron transfer moiety.

Burrows teaches the equivalence of a variety of transition metals in cleavage of DNA (see column 3, lines 3-5). Burrows expressly teaches that "The useful transition metals include ions of Ni, Co, Cu, Rh, Pd, Ir, Pt, Cr, Mn, Fe, Ru, and Os (see column 11, lines 36-38)." So Burrows expressly teaches the use of Osmium (Os),

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Cobalt (Co), Palladium (Pd), Platinum (Pt) and suggests the equivalence of all transition metals, which would include Rhenium.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the transition metal complexes of Burrows since Burrows teaches the equivalence of these transition metals in nucleic acid cleavage compositions. MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. *In re Fout* , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)." Consequently, it would have been prima facie obvious to substitute the various equivalent transition metals for each other in the composition of Claim 3 of U.S. Patent No. 5,780,234 since the prior art recognized these metals as equivalents in nucleic acid cleavage as demonstrated by Burrows

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman
Primary Examiner
Art Unit 1634